NEW PATENT CLAIMS

1. A cell comprising a membrane receptor which comprises a ligand-binding section, a membrane-localization signal and a mediator section, where only when there is binding or, alternatively, only when there is a lack of binding of a ligand to the ligand-binding section is a structural change brought about with effects on the mediator section to result in binding of an effector protein or polypeptide, which is capable of activating a Ras or Ras-like signal pathway in the cell, to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), characterized in that the effector protein or polypeptide which is capable of activating a Ras or Ras-like signal pathway is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding to the component of the membrane possible, where appropriate via other proteins or polypeptides (adaptors).

2. A cell as claimed in claim 1, characterized in that the effector section which is capable of activating a Ras or Ras-like signal pathway is a guanine nucleotide exchange factor (GEF) or an active protein from the Ras family.

3. A cell as claimed in claim 2, characterized in that the effector section which is capable of activating a Ras or Ras-like signal pathway is the CDC25 protein from *Saccharomyces cerevisiae* or is derived from such a protein.

4. A cell as claimed in claim 2, characterized in that the effector section which is capable of activating a Ras or Ras-like signal pathway is an SOS

protein from a mammal or an SOS-like protein from any organism, or is derived from such a protein.

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5. A cell as claimed in any of claims 1 to 4, characterized in that the fusion protein required enzymatic modification before it can be bound to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and in that an enzymatic activity necessary for the enzymatic modification is activated only because of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section.

6. A cell as claimed in any of claims 1 to 5, characterized in that the membrane receptor is a transmembrane receptor, an enzyme-coupled receptor, a G-protein-coupled receptor, a 7-transmembrane receptor or an odor receptor (or olfactorial receptor).

7. A cell as claimed in any of claims 1 to 5, characterized in that the membrane receptor is a non-naturally occurring, synthetic membrane receptor.

8. A cell as claimed in claim 7, wherein the ligand-binding section is derived from a ligand-binding section of a naturally occurring receptor.

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9. A cell as claimed in any of claims 1 to 7, characterized in that the ligand-binding section comprises the ligand-binding section of a transmembrane receptor, of a G-protein-coupled receptor, of a 7-transmembrane receptor, of an odor receptor (or olfactorial receptor) or of a nuclear receptor, or is derived from the latter.

10. A cell as claimed in claim 7, characterized in that the ligand-binding section is derived from a ligand-binding section of a naturally occurring receptor and, in particular, from the ligand-binding

section of a transmembrane receptor, of a G-protein-coupled receptor, of a 7-transmembrane receptor, of an odor receptor (or olfactorial receptor) or of a nuclear receptor, by mutation, in particular by substitution, deletion, insertion and/or modification of one or more amino acids or groups of amino acids, or is a synthetic ligand-binding section generated by molecular modeling.

Sub A3

11. A cell as claimed in any of claims 1 to 10, characterized in that the mediator section comprises the cytoplasmic part of a G-protein-coupled receptor, sections thereof or an amino acid sequence derived therefrom.

12. A cell as claimed in claim 11, characterized in that the effector protein or polypeptide which is capable of activating a Ras or Ras-like signal pathway in the cell is in the form of a fusion protein of an effector section with an adaptor protein which can interact after the α subunit has dissociated off the heterotrimeric G-protein with the regions, which are freely accessible because of this, of the β and γ subunits of the G-protein which are associated with the mediator section, or with the α subunit of the heterotrimeric G-protein after dissociation off from the β and γ subunit of the G-protein or as a result of the dissociation of the heterotrimeric G-protein with the mediator section of the membrane receptor.

13. A cell as claimed in claim 12, characterized in that the fusion protein comprises an effector section and a GRK2 kinase or a GRK3 kinase.

14. A cell as claimed in claim 12, characterized in that the fusion protein comprises an effector section and an antibody which specifically recognizes and binds the β and γ subunits of the G-protein after the α subunit has dissociated off.

15. A cell as claimed in any of claims 12 to 14, characterized in that the effector section of the fusion protein comprises the sequence of an active Ras protein.

16. A cell as claimed in claim 11, characterized in that the mediator section comprises the cytoplasmic part of a G-protein-coupled receptor, sections thereof or an amino acid sequence derived therefrom, where the G-protein interacting with the cytoplasmic part of the G-protein-coupled receptor activates in the activated state a phosphatidylinositol 3-kinase (PI3K).

17. A cell as claimed in claim 16, characterized in that the effector protein or polypeptide which is capable of activating a Ras or Ras-like signal pathway in the cell is in the form of a fusion protein of an effector section with an Src homology 2 (SH2) or a pleckstrin homology (PH) domain.

18. A cell as claimed in any of claims 1 to 10, characterized in that the mediator section is able, as a result of the ligand binding or, alternatively, lack of ligand binding to the ligand-binding section, to bind one or more adaptor proteins via which the effector protein or polypeptide which is capable of activating a Ras or Ras-like signal pathway in the cell, in the form of a fusion protein of an effector section with an adaptor protein or polypeptide section which makes binding possible to the component of the membrane via one or more of the adaptor proteins, can bind to the mediator section.

19. A cell as claimed in claim 18, characterized in that the mediator section is put in a position, as a result of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section, of exerting an enzymatic activity.

20. A cell as claimed in claim 19, characterized in that the mediator section is put in a position, as a result of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section, of exerting a tyrosine kinase activity, a serine/threonine kinase or phosphatase activity.

21. A cell as claimed in claim 20, characterized in that the mediator section comprises the cytoplasmic part of the EGFR (epidermal growth factor receptor) or is derived from the latter.

22. A cell as claimed in claim 18, characterized in that the ligand-binding section is put into a position, as a result of a binding or, alternatively, lack of binding of a ligand for this ligand-binding section, of activating a separate, receptor-specific enzyme.

23. A cell as claimed in claim 22, characterized in that the separate, receptor-specific enzyme is heterologous to the cell.

24. A cell as claimed in claim 22 or 23, characterized in that the separate receptor-specific enzyme is a kinase and, in particular a tyrosine kinase.

25. A cell as claimed in any of claims 18 to 24, characterized in that the adaptor proteins Gbr2 or Shc can be bound by the mediator section as a result of the ligand binding or, alternatively, lack of ligand binding to the ligand-binding section.

26. A cell as claimed in any of claims 1 to 25, characterized in that the cell is a prokaryotic or eukaryotic cell.

27. A cell as claimed in claim 26, characterized in that the cell is a eukaryotic cell and, in particular,

a yeast cell, specifically a yeast cell lacking cell walls.

28. A cell as claimed in any of claims 1 to 27, characterized in that it is applied to a solid carrier.

29. A cell as claimed in claim 28, characterized in that the cell is immobilized on biochips or enclosed in microchambers.

30. A cell as claimed in any of claims 1 to 29, characterized in that in the absence of the membrane receptor at least under certain conditions a Ras or Ras-like signal pathway in the cell cannot be activated.

31. A cell as claimed in claim 30, characterized in that the activatability of the Ras or Ras-like signal pathway is temperature-dependent in the absence of the membrane receptor.

32. A cell as claimed in claim 31, characterized in that the lack of activatability of the Ras or Ras-like signal pathway in the absence of the membrane receptor above a particular temperature is derived from at least one mutation of a guanine nucleotide exchange factor intrinsic to the cell, which has the effect that the latter is incapable of functioning above the particular temperature.

33. A cell as claimed in claim 32, characterized in that the cells are cells of the *Saccharomyces cerevisiae* yeast strain cdc25-2 or are derived therefrom.

34. A cell as claimed in claim 31 or 32, characterized in that the lack of activatability of the Ras or Ras-like signal pathway in the absence of the membrane receptor above a particular temperature is derived from

at least one mutation of a Ras protein intrinsic to the cell, which has the effect that the latter is incapable of functioning above the particular temperature.

35. An *in vivo* assay for determining the suitability of a test substance as ligand for a ligand-binding section of a receptor, characterized by the following steps:

(a) contacting the test substance with cells as claimed in any of claims 30-34 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether activation of the Ras or Ras-like signal pathway has taken place,

where detection of the activation of the Ras or Ras-like signal pathway indicates the ability of the test substance to bind to the ligand-binding section.

36. An assay as claimed in claim 35, where step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the ability of the test substance to bind to the ligand-binding section.

37. An assay as claimed in claim 35, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for

cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the ability of the test substance to bind to the ligand-binding section.

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38. An *in vivo* assay for determining the suitability of a test substance as ligand for a ligand-binding section of a receptor, characterized by the following steps:

(a) contacting the test substance with cells as claimed in any of claims 30-34 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place,

(c) investigating cells employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of the test substance, where detection of the activation of the Ras or Ras-like signal pathway in the absence of the test substance and the inactivity of the Ras or Ras-like signal pathway in the presence of the test substance indicates the ability of the test substance to bind to the ligand-binding section.

39. An assay as claimed in any of claims 35 to 38, characterized in that the test substance is a naturally occurring substance and, in particular, an odorant,

flavoring, peptide, peptide hormone, protein, in particular cytokine, growth factor, neurotransmitter, non-protein- or -peptide-like hormone and/or a vitamin.

40. An assay as claimed in any of claims 35 to 38, characterized in that the test substance is a non-naturally occurring substance and, in particular, a synthetic derivative of a natural ligand or a poison, in particular dioxin.

41. An assay as claimed in claim 40, characterized in that the test substance is employed as fusion protein comprising a presumed ligand domain.

42. A screening method for unknown ligands of a particular receptor, characterized in that an assay method as claimed in any of claims 35 to 38 is employed for the screening.

43. An *in vivo* assay for detecting the presence of a ligand for a ligand-binding section of a receptor in a sample which possibly contains the latter, characterized by the following steps:
(a) contacting the sample with cells as claimed in any of claims 30-34 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,
(b) investigating whether activation of the Ras or Ras-like signal pathway has taken place,
where detection of the activation of the Ras or Ras-like signal pathway indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

44. An assay as claimed in claim 43, where step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

45. An assay as claimed in claim 43, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

46. An *in vivo* assay for detecting the presence of a ligand for a ligand-binding section of a receptor in a sample which possibly contains the latter, characterized by the following steps:
(a) contacting the sample with cells as claimed in any of claims 30-34 under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,
(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place,

(c) investigating cells employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of the sample, where a detection of the activation of the Ras or Ras-like signal pathway in the absence of the sample and the inactivity of the Ras or Ras-like signal pathway in the presence of the sample indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

47. A screening method for unknown ligands of a particular receptor in a sample, characterized in that an assay method as claimed in any of claims 43 to 46 is employed for the screening.

48. An *in vivo* assay for the quantitative determination of the concentration of a ligand for a ligand-binding section of a receptor in a sample which contains the latter, characterized by the following steps:

(a) contacting an aliquot of the sample with cells as claimed in any of claims 30-34 under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,

(b) detecting quantitatively the extent of the activation of the Ras or Ras-like signal pathway by direct or indirect means,

(c) measuring the concentration of the ligand in the sample by comparing the measured extent of activation

with corresponding values measured for known standard concentrations of the ligand.

49. An assay as claimed in claim 48, characterized in that the quantitative detection of the extent of activation of the Ras or Ras-like signal pathway in step (b) takes place indirectly by determining the amount present in the cells of a transcription or translation product of a reporter gene whose expression takes place only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, at a particular time or the expression rate of this reporter gene based on the transcription or translation product under said conditions, and in step (c) the measurement of the concentration of the ligand in the sample takes place by comparing the measured values with corresponding values measured for known standard concentrations of the ligand.

50. An assay as claimed in claim 48, characterized in that in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and the quantitative detection of the extent of the activation of the Ras or Ras-like signal pathway in step (b) takes place indirectly by determining the reproduction of the cells at a fixed time or the reproduction rate of the cells under said conditions, and in step (c) the measurement of the concentration of the ligand in the sample takes place by comparing the measured values with corresponding values measured for known standard concentrations of the ligand.

51. An *in vivo* assay for detecting whether a compound is able to alter a binding activity of a ligand-binding section of a receptor in relation to a ligand, characterized by the following steps:

(a) contacting the ligand in the presence of the compound with cells as claimed in any of claims 30 to 34 under conditions with which in the absence of the membrane receptor the Ras or Ras-like signal pathway in the cells cannot be activated, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of or, alternatively, the lack of binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 1, is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether and, where appropriate, to what extent activation of the Ras or Ras-like signal pathway takes place,

(c) comparing the result of the investigation in step (b) with a result of an investigation obtained when the assay is carried out in the absence of the compound.

52. An assay as claimed in claim 51, characterized in that step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, and the quantitative detection, which takes place where appropriate, of the extent of the activation of the Ras or Ras-like signal pathway comprises determining the amount, present in the cells, of transcription or translation product of the reporter gene at a particular time or the expression rate of this reporter gene based on the transcription or translation product under said conditions, and in the case where the comparison in step (c) reveals that stronger expression of the reporter gene occurs in the presence of the compound, an agonistic effect of the compound is indicated, and in the case where the comparison in (c) reveals that

lower expression of the reporter gene occurs in the presence of the compound, an antagonistic effect of the compound is indicated.

53. An assay as claimed in claim 52, characterized in that it is carried out under conditions with which no reproduction of the cells occurs.

54. An assay as claimed in claim 51, where in step (a) there is use of cells in which the inactive Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction, and step (b) comprises investigating whether and, where appropriate to what extent, the cells are able to reproduce under said conditions, and in the case where the comparison in step (c) reveals that greater cell reproduction occurs in the presence of the compound, an agonistic effect of the compound is indicated, and in the case where the comparison in step (c) reveals that less cell reproduction occurs in the presence of the compound, an antagonistic effect of the compound is indicated.

55. An *in vivo* assay for detecting whether a polypeptide or protein has a ligand-binding function of a receptor, characterized by the following steps:
(a) contacting cells as claimed in any of claims 30 to 34 with the ligand under conditions with which in the absence of the membrane receptor, as defined in claim 1, a Ras or Ras-like signal pathway in the cells cannot be activated, where the ligand-binding section of the membrane receptor comprises the polypeptide or protein to be investigated or consists thereof, and where the effector protein or polypeptide whose binding to a membrane component depends on the binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway,

(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place,
where detection of the activation of the Ras or Ras-like signal pathway indicates that the ligand-binding section of the membrane receptor and, accordingly, the polypeptide or protein to be investigated has a ligand-binding function of a receptor.

56. An assay method as claimed in claim 55, characterized in that the ligand-binding section of the membrane receptor present in the cells is derived from a naturally occurring receptor section by mutation.

57. An assay as claimed in claim 55 or 56, where step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the ligand-binding function of the ligand-binding section of the membrane receptor and, accordingly, of the polypeptide or protein to be investigated.

58. An assay as claimed in claim 55 or 56, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the ligand-binding function of the ligand-binding section of the membrane receptor and, accordingly, of the polypeptide or protein to be investigated.

59. An *in vivo* assay for detecting whether a polypeptide or protein has a ligand-binding function of a receptor, characterized by the following steps:
(a) contacting cells as claimed in any of claims 30 to 34 with the ligand under conditions with which in the absence of the membrane receptor, as defined in claim 1, a Ras or Ras-like signal pathway in the cells cannot be activated, where the ligand-binding section of the membrane receptor comprises the polypeptide or protein to be investigated or consists thereof, and where the effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway,
(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place,
(c) investigating cells as employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of ligands,
where a detection of the activation of the Ras or Ras-like signal pathway in the absence of the ligand and the inactivity of the Ras or Ras-like signal pathway in the presence of the ligand indicates that the ligand-binding section of the membrane receptor and, accordingly, the polypeptide or protein to be investigated has a ligand-binding function of a receptor.

60. A kit for use in an assay as claimed in any of claims 35 to 54, which comprises cells as claimed in any of claims 30-34.

SIPPEL, Albrecht, E. et al.
07 February 2001

NEW PATENT CLAIMS 61 - 70

61. A kit for use in an assay as claimed in any of claims 35 to 54, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which at least under certain conditions a Ras or Ras-like signal pathway cannot be activated;

(b) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes a membrane receptor, as defined in claim 1, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

AMENDED SHEET

62. A kit for use in an assay as claimed in any of claims 35 to 54, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;

(b) a nucleic acid vector which comprises, in suitable arrangement:

- a DNA section which encodes a membrane-localization signal of a membrane receptor, as defined in claim 1;
- a DNA section which encodes a mediator section of a membrane receptor, as defined in claim 1; and
- a suitably arranged insertion site for functional insertion of a DNA sequence which encodes a ligand-binding section, as defined in claim 1,

where, after insertion of a DNA sequence for the ligand-binding section, the nucleic acid vector comprises a complete expressible gene for a membrane receptor, as defined in claim 1, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

63. A kit for use in an assay as claimed in any of claims 55 to 59, which comprises cells as claimed in any of claims 30-34, where the membrane receptor, as defined in claim 1, present therein comprises a ligand-binding section comprising or consisting of a polypeptide or protein suspected of having a ligand-binding function of a receptor.

64. A kit for use in an assay as claimed in any of claims 55 to 59, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:
(a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;
(b) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes a membrane receptor, as defined in claim 1, where the ligand-binding section of the membrane receptor comprises a polypeptide or protein suspected of having a ligand-binding function of a receptor, or is formed therefrom, and the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under a);
(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is

able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

65. A kit for use in an assay as claimed in any of claims 55 to 59, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;

(b) a nucleic acid vector which comprises, in suitable arrangement:

- a DNA section which encodes a membrane-localization signal of a membrane receptor, as defined in claim 1;
- a DNA section which encodes a mediator section of a membrane receptor, as defined in claim 1; and
- a suitably arranged insertion site for functional insertion of a DNA sequence which encodes a polypeptide or protein suspected of having a ligand-binding function of a receptor,

where, after insertion of a DNA sequence for the ligand-binding section, the nucleic acid vector comprises a complete expressible gene for a membrane receptor, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to a ligand-binding section, formed from the

polypeptide or protein suspected of having a ligand-binding function of a receptor, of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

66. A kit as claimed in any of claims 60 to 65, in which the cells additionally contain a construct comprising a binding site for a transcription factor whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and a reporter gene functionally linked thereto, where the minimal promoter is activated as a result of binding of the activated transcription factor to its binding site.

67. A kit as claimed in any of claims 60 to 65, characterized in that it additionally contains a transformation or transfection vector with a construct comprising a binding site for a transcription factor

whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and a reporter gene functionally linked thereto, where the minimal promoter is activated as a result of a binding of the activated transcription factor to its binding site.

68. A kit as claimed in any of claims 60 to 65, characterized in that it additionally contains a transformation or transfection vector with a construct comprising a binding site for a transcription factor whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and an insertion site, suitably arranged for expression controlled by the minimal promoter, for insertion of a reporter gene, where the minimal promoter is activated as a result of a binding of the activated transcription factor to its binding site.

69. A kit as claimed in any of claims 60 to 68, which contains the cells immobilized or enclosed in microchambers of a solid carrier, in particular on biochips.

70. A method for identifying polypeptides or proteins, in particular receptors, which have a ligand-binding function of a receptor, which comprises:

- preparing a cell as claimed in claim 1 with a membrane receptor having the features described in claim 1 and comprising the whole of such a polypeptide or protein or a part of such a polypeptide or protein which presumably contains the sequence sections essential for the ligand-binding function, and
- using this cell to carry out an *in vivo* assay method for detecting whether a polypeptide or

protein has a ligand-binding function of a receptor, as claimed in any of claims 55 to 59.